TRIAMCINOLINE ACETONIDE (KENALOG) IN TREATMENT OF CASES OF HAY FEVER AND ITS EFFECT ON PITUITARY-ADRENAL AXIS

by

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INTRODUCTION

Since 1949, when Hench and Kendall introduced the use of cortisone and hydrocortisone, a voluminous literature has accumulated concerning the employment of these agents in allergic diseases. Steroid therapy requires careful thought in view of the evidence that long term treatment can react adversely on the pituitary-adrenal axis. Nevertheless, an injectable steroid may be used in the treatment of chronic hay fever, and I have undertaken a trial in my own practice. In this small series of cases a study of the clinical effects, and a laboratory investigation of adrenal function are compared.

Hay fever is a hypersensitive state characterised by hyperactivity of the body to contact with a foreign substance in an amount which would not disturb a non-allergic individual. Allergy is a chronic and progressive disease, but hyposensitisation in some way alters the basic hypersensitivity and thereby helps to prevent the allergic symptoms from being multiple. Total avoidance of exposure to the incriminating allergen is usually impossible as it is airborne and inhaled, so hyposensitisation is the more practicable treatment. However, not every chronic case responds to this desensitisation programme, and in addition, it is time consuming for the patient and doctor alike, and new methods have to be explored which may be more efficacious.

Hay fever has been treated with a variety of adrenocorticosteroids. Much research has been performed to develop new adrenocorticosteroids which would possess greater biological activity and maintain an adequate ratio of glucocorticoid to mineralocorticoid activity. Alterations in the chemical configurations of the steroid nucleus and its chains produced triamcinolone. 16 – α – hydroxlyation markedly decreased mineralocorticoid activity and abolished the sodium retaining properties of 9 – α – fluorosteroids without destroying their glucocorticoid activity. It is one and a half to two times more potent than prednisolone. The greater therapeutic activity of triamcinolone is not accompanied by a corresponding increase in production of adverse effects. Triamcinolone Acetonide (the corticosteroid used in this trial) suppresses the clinical manifestation of hay fever and affords symptomatic relief. The mechanism of action is not entirely clear. In allergic conditions the union of antigen and antibody acts as a stress and either alone, or with the stress stimuli, e.g., psychogenic influences or infection, causes a liberation of histamine, acetyl choline, serotonin, and unknown substances which trigger allergic tissue responses. The exact mode of action is not clearly understood. It is suggested that they act locally upon the sensitised tissue cells, decrease the reactivity of the shock organs to specific antigens and stress and suppress local tissue responses rendering the cells less subject to injury. They increase permeability

and prevent formation of oedema and granulation tissue. Triamcinolone decreases oedema and increases the permeability of basement membrane. This is interpreted as being caused by the arrest of muco-protein breakdown and restoration of the normal state.

Design

The aim of this study was to test the efficacy and note any adverse reactions of triamcinolone acetonide following one 80 mg I-M injection in the gluteus maximus in patients with hay fever.

Patients included in the trial were between the ages of 25 and 45 and were of both sexes. They had symptoms of seasonal hay fever this year and also a history of severe seasonal hay fever over a minimum of three years which had responded poorly to other medicaments, e.g., antihistamines. Patients with a history of tuberculosis, hypertension, diabetes and duodenal ulcer were excluded. All patients were otherwise in good health and apyrexic.

The use of any exogenous steroid will affect the pituitary-adrenal axis. It was therefore decided to estimate cortisol levels at specific times following the injection. Each patient had cortisol estimated by withdrawal of blood from a vein in the antecubital fossa before the injection of 80 mg. triamcinolone acetonide was given intramuscularly in the gluteus maximus. Cortisol estimations were carried out at 24 hours, 48 hours, 7 days, 14 days, and 21 days after the injection. Response to injection was noted at each interview and patients were given a diary card to record symptoms of hay fever and/or side effects. Only patients who were willing and able to attend for repeated investigations at a fixed time – viz. 10 a.m., were studied. The time factor was considered very important as it is well known that cortisol levels vary along a 24 hours phasing scale under conditions standardised to eliminate stimulation other than daily routine.

The range of normal values of any body constituent, a time honoured standard, does not take into account the specific time at which the level was determined but rather allows for the existing variability of body function throughout the 24 hours. Circadian rhythms contribute largely to normal variations and this physiological regulation must be understood if disturbances of health are to be recognised and interpreted, and thus prevented or corrected. Depending on their time dimension, circadian rhythms either hinder or further studies in adaptive responses, and must to some extent dictate the experimental approach. Possibly the simplest approach is to attempt to eliminate their effect by fixed sampling times as is done in this series. The adrenal cycle is modulated by superimposed or juxtaposed endocrines and the interactions involved await further study. This field of study has a long history and has been reviewed repeatedly (Conroy and Mills, 1970).

The method of cortisol estimation used was that described by Mattingly (1962). The preparation under study was an aqueous suspension of triamcinolone acetonide, each ml. containing 40 mg of the corticosteroid with sodium chloride for isotonicity, 0.9 per cent benzyl alcohol as a preservative, and 0.75 per cent sodium caboxymethyl cellulose, and 0.04 per cent polysorbate 80 as excipients. 2 ml. of this preparation was administered intramuscularly to each patient of the series, injections being given into the gluteal muscle in every case.

Results

Clinical results were regarded as excellent in 12 of the 18 cases whose symptoms subsided rapidly, usually within 12 to 48 hours after injection, and did not reappear thereafter, so that no further supportive therapy was required. The clinical results were considered as good in five additional patients. In these patients there was marked symptomatic relief following the injection of triamcincolone acetonide although very mild symptoms recurred which required no further supportive treatment. One patient had a recurrence of his hay fever four weeks after the initial injection which necessitated further therapy. Response of three patients who in previous years had received desensitisation injections was dramatic and much appreciated, in that only one injection was required. The remaining 15 patients, who in previous years had antihistamines, were relieved since they were no longer drowsy at work. Side effects were negligible in the series. Three patients remarked on flushing of the face within 36 hours of injection.

The clinical benefits from this series compare favourably with the smaller series treated with two 80 mg. doses of methyl prednisolone acetate given at an interval of two weeks (Ganderton and James, 1970).

The cortisol estimations show depression of the pituitary adrenal axis within 24 hours. This lasted for varying times, but within three weeks the cortisol level returned to its initial level. Individual variations can be seen and response to emotional factors may explain the elevated levels in one case at two weeks in comparison with three weeks after the injection. The table shows the actual cortisol

Table

Cortisol Level mgs. per cent

Sex	*Age*	*Before injection*	*24 hrs. after*	*48 hrs. after*	*1/52 after*	*2/52 after*	*3/52 after*
M	39	10	4	3	3.5	4	9
M	28	21	9.5	4	2.5	3.5	17
M	31	10.5	8	5	2	3	10
M	28	21	9	5	2	21	31
M	34	13	9	5	5.5	9	27
M	40	9.5	2	2	7	9.5	10
M	32	15	6.5	5	9.5	9.3	17
M	32	17.5	5.5	4	9.5	9	14.5
M	45	11.5	4.5	2	3.5	9.5	13.5
F	26	7	3.5	2	5.5	8	9.5
F	28	19	14	9.5	8.5	12	13.5
M	35	7	5	2	7.5	12	16
M	35	13	9	5	7	9	11
F	26	9	2	2	5	9	10
M	27	15	8.5	3	7.5	11	13.5
M	25	11	4	2	4.5	9	10
F	26	14.5	7	4	9.5	9	13.5
F	28	17.5	6	2	7	9.5	16

levels obtained. This part of the study was thought to be of particular importance as any long-term influence on the pituitary-adrenal axis would be a definite drawback to the widespread use of triamcinolone acetonide injections for hay fever. It would appear from this study that recovery from adrenal suppression occurred in every case.

The small incidence of side effects may be attributed to the strict criteria used for selecting the personnel in the trial, and I feel that in the future, more use may be made of triamcinolone acetonide in this type of susceptible hay fever victim.

Summary

The use of a synthetic corticosteroid in the treatment of hay fever is described and the effects of the treatment on adrenal function are considered. It is sugested that treatment with triamcinolone can be of value to the susceptible hay fever sufferer.

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